REMARKS

Formal Matters

Claims 8-25 are pending.

Claims 8-25 were examined and rejected. No claims were allowed.

Claims 8 and 21-23 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to the claims is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: page 3, lines 9-14; page 3, lines 6-11; page 6, line 12; page 4, lines 25-26; page 15, lines 14-20; page 7, lines 4-6 and page 8 lines 7-23.

No new matter is added by these amendments.

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

Interview summary

The Applicants wish to express their gratitude to Examiner Brusca for the interview on September 8, 2004, with Applicants' representatives James Keddie, Carol Francis and Jim Diehl.

All current rejections were discussed, as well as arguments to overcome those rejections. Applicants arguments were advanced in the communication filed with the Office on July 16, 2004, and are further elaborated herein.

Examiner Brusca agreed that the concept of a cellular component that is not produced using a nucleic acid made using recombinant DNA technology is implicitly set forth in the instant specification. As such, the instant specification supports the amendments made herein.

PTO/SB/08A form

The Applicants gratefully acknowledge receipt of the initialed PTO/SB/08A form indicating that the information listed therein has been considered and made of record.

Obviousness-type double patenting rejections

The Applicants gratefully acknowledge withdrawal of the obviousness-type double patenting rejections

Rejection of claims under 35 U.S.C. § 103(a)

Claims 8-20 are again rejected under 35 U.S.C. § 103(a) as unpatentable over Yang in view of Fearon, Rayner and Gonda. Specifically, the Office asserts that Yang's yeast random peptide two hybrid methods, in combination with Fearon's mammalian two-hybrid system, Rayner's retroviral vector cDNA library and Gonda's N-terminal glycine, render claims 8-20 unpatentable.

Without any intention to acquiesce to the correctness of the rejection and solely to expedite prosecution, the claims have been amended to recite screening for a cell exhibiting an altered phenotype due to **an interaction between a test peptide and a cellular protein that is *not* produced using a nucleic acid made using recombinant DNA technology**. The Applicants respectfully submit that none of the cited references disclose this feature, and, accordingly, this rejection may be withdrawn.

The primary references in this rejection are Yang and Fearon. Both of these references describe "two hybrid" assays which, as is well known in the art, are used for testing binding of two fusion proteins in a cell. Both of these fusion proteins are produced using a nucleic acid made using recombinant DNA technology and, as such, both of Yang and Fearon's methods involve screening for a phenotype produced by an interaction between two proteins each produced using a nucleic acid made using recombinant DNA technology.

Accordingly, Yang and Fearon's disclosures are deficient in that they do not disclose detecting binding between a test peptide and a cellular protein that is ***not*** produced using a nucleic acid made using recombinant DNA technology, as required by the rejected claims.

In this rejection, Rayner and Gonda are cited solely to provide a retroviral vector cDNA library and an N-terminal glycine, respectively. Rayner's retroviral vector cDNA library and Gonda's N-terminal glycine fail to cure the deficiencies of Yang and Fearon discussed above. Accordingly, Yang, Fearon, Rayner and Gonda, either alone or in any combination, fail to teach or suggest detection of an altered phenotype that is due to an interaction between a test peptide and a cellular protein that is *not* produced using a nucleic acid made using recombinant DNA technology, as required by the rejected claims.

In view of the foregoing discussion, the Applicants respectfully submit that this rejection has been adequately addressed and may be withdrawn.

Furthermore, the Applicants further note that in a two hybrid assay any molecular interaction between a protein encoded by two-hybrid vector and a "native"[1] protein in a cell would mask interactions between the components of the two-hybrid system, reduce the expression of the reporter protein and would probably ruin the assay. Molecular interactions with native proteins are absolutely undesirable in a two-hybrid assay.

Since what is being claimed is an assay for detecting a molecular interaction with a native protein, the Applicants respectfully submit that two-hybrid system-related art, including the disclosures of Yang and Fearon, teach directly away from the claimed invention.

Accordingly, even if the Office attempts to reject the claims over two-hybrid system-related art in a way not set forth in the Office Action, a proper *prima facie* case of obviousness could not be established.

Finally, the Applicants further submit that Rayner merely discloses a cellular assay by which cDNAs are introduced into cells that are then screened for a particular phenotype. Rayner makes no mention of detecting interactions between a test peptide and a native protein and Rayner's assay is not designed to detect an interaction between a test peptide and a native protein. In fact, Rayner's assay could not be readily adapted to be an assay for detecting such an interaction.

Accordingly, even if the Office attempted to reject the instant claims by combining the teachings of Raynor, Yang and Fearon in a way that is not set forth in the Office Action, the resulting combination of references would still fail to provide a *prima facie* case of obviousness because the resulting combination would still fail to disclose an element of the claims: an altered phenotype due to an *interaction between a test peptide and a cellular native protein.*

The Applicants also note that Rayner's disclosure is sharply focused on the identification of *cDNA-encoded proteins* that produce a particular phenotype. As would be recognized by one of skill in the art, cDNA-encoded proteins are encoded by the genome of a cell and have a specific biological

[1] By "native" is meant a protein that is *not* produced using a nucleic acid made using recombinant DNA technology as recited in the claims.

activity. In order to provide this activity, cDNA-encoded proteins contain a defined sequence of amino acids. The amino acid sequence of a cDNA-encoded protein defines the activity of the protein.

In contrast to the cDNA-encoded proteins of Rayner, the rejected claims are focused on peptides having a *randomized* sequence of amino acids. Conceptually, such peptides are as far from those of cDNA-encoded protein as possible.

At no point does Rayner suggest methods for identifying proteins other than cDNA-encoded proteins, and, as such, Rayner provides no motivation to provide the claimed invention. In fact, Rayner's general teachings, in particular the phrase "retrovirus cloning can be used to isolate any **cDNA** for which a functional screen can be devised" (see Rayner's last paragraph; emphasis added) would lead one of skill in the art away from the invention. In other words, Rayner suggests that his method can be adapted for other situations where one *knows that a particular protein exists* and further *knows how to assay for that protein.* Rayner's suggestion would likely point one of skill in the art directly *away* from the claimed invention since, as discussed above, Rayner's cDNA-encoded proteins contain a *defined* sequence of amino acids and the claim-recited peptides contain a *random* sequence of amino acids. One need not know in advance that a random peptide exists that can elicit a desired effect on the cell. Indeed, the point of the claimed method is that it can be used to identify random peptides having a desired activity where the random peptides have no previously known function.

The Applicants respectfully submit that the combination of Fearon with a two hybrid system-related reference provides, at best, a two-hybrid assay that employs a retroviral vector. Such an assay is not what is not what is being claimed.

The Applicants respectfully submit that this rejection has been adequately addressed by the foregoing discussion. Withdrawal of this rejection and allowance of claim 8-20 is respectfully requested.

Claims 21-23 are rejected under 35 U.S.C. § 103(a) as unpatentable over Yang in view of Fearon, Rayner and Kaufmann. Specifically, the Office asserts that Yang's random peptide two hybrid methods in yeast, in combination with Fearon's two-hybrid system in a mammalian cell, Rayner's retroviral vector cDNA library and Kaufmann's cell survival methods, render claims 21-23 unpatentable. This rejection is respectfully traversed as applied and as it may be applied to the amended claims.

As discussed above, Yang, Fearon and Rayner either alone or in combination fail to teach or suggest assaying an interaction between a test peptide and a cellular protein that is *not* produced using a nucleic acid made using recombinant DNA technology.

Kaufmann is cited solely to provide a method of detection of cell survival. Kaufmann's cell survival method fails to cure the deficiencies of Yang, Fearon and Rayner. Accordingly, Yang, Fearon, Rayner and Kaufmann, either alone or in any combination, fail to teach or suggest assaying an interaction between a test peptide and a cellular protein that is *not* produced using a nucleic acid made using recombinant DNA technology.

Withdrawal of this rejection is respectfully requested.

Claims 24 and 25 are rejected under 35 U.S.C. § 103(a) as unpatentable over Yang in view of Fearon, Rayner, Kaufmann and Abbas. Specifically, the Office asserts that Yang's random peptide two hybrid methods in yeast, in combination with Fearon's two-hybrid methods in a mammalian cell, Rayner's retroviral vector cDNA library, Kaufmann's cell survival methods and Abbas' methods of detecting cell differentiation render claims 24 and 25 unpatentable. This rejection is traversed as applied and as it may be applied to the amended claims.

As discussed above, Yang, Fearon and Rayner either alone or in combination fail to teach or suggest assaying an interaction between a test peptide and a cellular protein that is *not* produced using a nucleic acid made using recombinant DNA technology. Also as discussed above, Kaufmann fails to cure these deficiencies of Yang, Fearon and Rayner.

Abbas is cited solely to provide methods of detecting cell differentiation. Abbas fails to cure the deficiencies of Yang, Fearon, Rayner and Kaufmann. Accordingly, Yang, Fearon, Rayner, Kaufmann and Abbas, either alone or in any combination, fail to teach or suggest assaying an interaction between a test peptide and a cellular protein that is *not* produced using a nucleic acid made using recombinant DNA technology.

Withdrawal of this rejection is respectfully requested.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RIGL-005CON.

Respectfully submitted,
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Date: September 23, 2004

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